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| 10/714,506 | 11/13/2003 | Sanjay Awasthi | 124263-1007 | 1056 |

7590 12/18/2006

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| EXAMINER | |
|---|---|
| FETTEROLF, BRANDON J | |
| ART UNIT | PAPER NUMBER |
| 1642 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
|---|---|---|
| 3 MONTHS | 12/18/2006 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

TH

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/714,506 | AWASTHI ET AL. | |
| | Examiner | Art Unit | |
| | Brandon J. Fetterolf, PhD | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *03 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *3 and 12-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 4-11 and 19-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/03/2006 has been entered.

Claims 1-20 are currently pending and under consideration.

Claims 12-18 are withdrawn from consideration as being drawn to non-elected inventions.

Claim 3 has been withdrawn by Applicants.

Claims 1-2, 4-11 and 19-20 are currently under consideration.

### *Response to Amendment*

The Declaration Under CFR 1.131 filed on 10/03/2006 has been considered but is ineffective to overcome the rejection of claims 1 and 3-9 under 35 U.S.C. 102(a) as being anticipated by Awasthi *et al.* (Proc. Am. Assoc. Cancer. Res. March 2002; 43: Abs.) As stated in the previous office action, the Examiner acknowledges that Applicants have provided an appropriate oath or declaration to establish invention of the subject matter of the rejected claims prior to the effective date of the reference or activity on which the rejection is based. However, the Examiner recognizes that Applicants have provided no facts, i.e., original exhibits of drawings or records, or photocopies thereof, which must accompany and form part of the affidavit or declaration, see MPEP, CFR 1.131.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 4-9 are rejected under 35 U.S.C. 102(a) as being anticipated by Awasthi *et al.* (Proc. Am. Assoc. Cancer. Res. March 2002; 43: Abs. *of record*) as evidenced by Sharma *et al.* (Arch. Biochem. Biophys. 2001; 391: 171-179 *of record*).

Awasthi *et al.* teach a method of treating 6 NSCLC cell lines undergoing uncontrolled growth comprising contacting the cells with polyclonal RLIP76 antibodies, wherein the administration of the antibodies results in apoptosis. Moreover, the reference discloses that the method further comprises administering a drug used in chemotherapy, e.g., doxorubicin, in combination with the antibody, wherein the addition of the drug to the antibody enhanced the cytotoxicity of the drug. In addition to doxorubicin, Awasthi *et al.* also teach that the combination of Herceptin and anti-RLIP76 resulted in an additive effect with regards to cytotoxicity. Although Awasthi et al does not specifically teach that the antibody to RLIP76 blocks the function of the RalA binding protein 1 and prevents a drug from leaving the cell, the claimed functional limitation would be an inherent property of the referenced method because as evidenced by Sharma *et al.,* ATP dependent inhibition of the ATP-dependent transport of DOX was inhibited in erythrocyte inside-out vesicles coated with antibodies against RLIP76 (Abstract). Thus, it does not appear that the claim language or limitation results in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001). The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed method. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Moreover, even though the claims are drawn to a mechanism by which the antibody treats cancer cells, the claimed method does not appear to distinguish over the prior art teaching of the same or nearly the same method. The mechanism of action does not have a bearing on the

patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

In response to this rejection, Applicants have submitted a signed Declaration under 37 CFR 1.131 by the Applicants establishing that the Awasthi 2002 reference is describing Applicant's own work. Moreover, Applicants submit that they have provided documentary evidence that accompany the affidavit to show that they conceived and reduced to practice in the United States of America the invention as shown and described in the above-identified application prior to the date of March 2002, the date of publication of Awasthi 2002. For example, Applicants assert that the evidence, provided as Exhibit A, is a document that describes the methods of the claimed invention and further, provides evidence that they reduced to practice the invention as described and claimed in the above-identified application in the United States of America prior to March 2002. Accordingly, Applicants submit that the subject matter considered prior art under 35 USC 102 (a) is now disqualified as prior art against this Application for invention.

The Declaration Under CFR 1.131 filed on 10/03/2006 has been considered but is ineffective to overcome the Awasthi *et al.* reference. In the instant case, the Examiner acknowledges that Applicants have provided an appropriate oath or declaration to establish invention of the subject matter of the rejected claims prior to the effective date of the reference or activity on which the rejection is based. However, the Examiner recognizes that Applicants have provided no facts, i.e., original exhibits of drawings or records, or photocopies thereof, which must accompany and form part of the affidavit or declaration, see MPEP, CFR 1.131. As such, Claims 1 and 3-9 remain rejected under 35 U.S.C. 102(a) as being anticipated by Awasthi *et al.* (Proc. Am. Assoc. Cancer. Res. March 2002; 43: Abs.) For example, Exhibit A, which Applicants contend describes the methods of the claimed invention, appears to be a correspondence to Dr. Larry Matherly suggesting that 14 figures along with figure legends for an abstract are being sent. However, these figures and described methods as claimed do not appear to be attached to Exhibit A. Thus, claims 1 and 4-9

remain rejected under 35 U.S.C. 102(a) as being anticipated by Awasthi *et al.* (Proc. Am. Assoc. Cancer. Res. March 2002; 43: Abs.).

Claims 1 and 4-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Awasthi *et al.* (Proc. Am. Assoc. Cancer. Res. March 2001; 42: Abst. *of record*) as evidenced by Sharma *et al.* (Arch. Biochem. Biophys. 2001; 391: 171-179 *of record*).

Awasthi *et al.* teach a method of treating both SCLC and NSCLC cell lines undergoing uncontrolled growth comprising contacting the cells with anti-RLIP76 antibodies which recognize a cell surface epitope in lung cancer cells. The reference further teaches that the administration of anti-RLIP76 to the cells resulted in DNA laddering demonstrating apoptotic activity. Moreover, Awasthi *et al.* discloses that the method further comprises administering a drug used in chemotherapy, e.g., doxorubicin, in combination with the antibody, wherein the addition of the drug to the antibody enhanced the cytotoxicity of the drug. Although Awasthi et al does not specifically teach that the antibody to RLIP76 blocks the function of the RalA binding protein 1 and prevents a drug from leaving the cell, the claimed functional limitation would be an inherent property of the referenced method because as evidenced by Sharma *et al.* ATP dependent inhibition of the ATP-dependent transport of DOX was inhibited in erythrocyte inside-out vesicles coated with antibodies against RLIP76 (Abstract). Thus, it does not appear that the claim language or limitation results in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001). The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed method. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Moreover, even though the claims are drawn to a mechanism by which the antibody treats cancer cells, the claimed method does not appear to distinguish over the prior art teaching of the same or nearly the same method. The mechanism of action does not have a bearing on the

patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

In response to the rejection, Applicants submit that claim 1 has been amended to recite a method of "treating one or more cells undergoing uncontrolled growth comprising the steps of contacting one or more cells with an antibody to ralA biding protein1, wherein the direct contact is cytotoxic to one or more cells in the absence or an additional agent and wherein the antibody blocks the function of the ralA binding protein 1." (Emphasis indicating amended text). As such, Applicants contend that Awasthi 2001 does not disclose or suggest amended claim 1, including wherein the antibody blocks the function of ral1A binding protein 1. Instead, Applicants assert that Awasthi 2001 discloses, "Antibodies markedly augment the cytotoxicity of doxorubicin," which this is not equivalent to the antibodies themselves being cytotoxic. For example, Applicants submit that the Examiner asserts that Awasthi 2001 teaches administrations of anti-RLIP76 alone to SCLC and NSCLC cells results in DNA laddering; however, Applicants submit that this is not conclusive of cytotoxicity, since some DNA laddering may always be found in cancer-like cells such as SCLC and NSCLC cells, which is quite clear since Awasthi 2001 further described that it is only when doxorubicin in combination with an antibody are applied to such cells that "DNA laddering was... significantly increased." Applicants further submit that the Examiners assertion that Awasthi 2001 "teaches that the anti-RLIP76 antibodies are useful as therapeutic modality." is only a speculation and not a teaching with any predictability which can not be used as evidence for a teaching of the claimed inventions

These arguments have been carefully considered, but are not found persuasive.
In response to Applicant's contention that Awasthi 2001 does not teach or suggest amended claim 1 including blocking the function of ralA binding protein 1, the Examiner acknowledges, as stated above, the Awasthi does not specifically teach that the antibody block the function of ralA binding protein 1. However, the Examiner recognizes the claimed limitation would be an inherent property of the referenced method because as evidenced by Sharma *et al.* (Arch.

Biochem. Biophys. 2001; 391: 171-179) ATP dependent inhibition of the ATP-dependent transport of DOX was inhibited in erythrocyte inside-out vesicles coated with antibodies against RLIP76 (Abstract). In other words, antibodies against RLIP76 (ralA biding protein 1) inhibit the ATP-dependent transport of DOX, e.g., block the transport function of RLIP76. As noted above, the office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed method. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989) (*emphasis added*). With respect to Applicants assertions pertaining to DNA laddering and quotation of Awasthi 2001, the Examiner has reviewed the Awasthi 2001 reference but cannot find clear support for what Applicants assert Awasthi et al. teach. For example, Awasthi 2001 teach "In both SCLC and NSCLC, DNA laddering was observed with antibody alone, doxorubicin alone, and significantly increased in presence of both." Thus, it is unclear how these teachings support Applicants assertions that DNA laddering may always be found in cancer-like cells such as SCLC and NSCLC cells. Regarding Applicants assertions that speculation is not a teaching with any predictability, the Examiner acknowledges that Awasthi et al. teach that "anti-RLIP76 antibodies may be useful as a therapeutic modality for lung cancer, both alone and in combination with chemotherapy." However, the Examiner recognizes that even if speculations cannot be used as evidence, the method steps of the instant claims, e.g., contacting one or more cells with an antibody to ralA binding protein 1, are clearly anticipated by Awasthi 2001 teachings of contacting one or more cells with an antibody to RLIP76, wherein the antibodies induce apoptosis. As such, claims 1 and 4-9 remain rejected under 35 U.S.C. 102(b) as being anticipated by Awasthi *et al.* (Proc. Am. Assoc. Cancer. Res. March 2001; 42: Abst.) as evidenced by Sharma *et al.* (Arch. Biochem. Biophys. 2001; 391: 171-179).

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Awasthi *et al.* (Proc. Am: Assoc. Cancer. Res. March 2001; 42: Abst. *of record*) in view of American Type Culture Collection (Tumor Cell Lines, 2001 *of record*).

Awasthi *et al.* teaches, as applied to claims 1 and 4-9 above, a method of treating both SCLC and NSCLC cell lines undergoing uncontrolled growth comprising contacting the cells with anti-RLIP76 antibodies which recognize a cell surface epitope in lung cancer cells.

Awasthi *et al.* does not teach that the cells are selected from the group of cancerous cells consisting of NCI-H82, NCI-H182, NCI-1417, NCI-1618, NCI-H1395, NCI-H2347, HCC44 (adenocarcinoma), and NCI-H2126.

American Type Culture Collection discloses a plethora of commercially available tumor cell lines including but not limited cell lines obtained from SCLC and NSCLC such as NCI-H82, NCI-1417, NCI-1618, NCI-H1395, NCI-H2341 and NCI-H2126.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use a SCLC or NSCLC tumor cell line in the method of Awasthi *et al.*. One would have been motivated to do so because the American Type Culture Collection discloses commercially available lung tumor cell lines, SCLC and NSCLC, while Awasthi *et al.* teaches a method of treating SCLC and NSCLC cell lines undergoing uncontrolled cell growth with RLIP76 antibodies which specifically recognize an epitope in lung cancer cells. Thus, one of ordinary skill in the art would have a reasonable expectation of success that by combining a SCLC or NSCLC tumor cell line available through ATCC with the method as taught by Awasthi et al., one would achieve a method of treating uncontrolled cell growth in at least NCI-H82, NCI-1417, NCI-1618, NCI-H1395, NCI-H2341 and NCI-H2126 cells.

In response to this rejection, Applicants contend claims 1-9 are not anticipated by Awasthi 2001 for the reasons set forth above and therefore, combining Awasthi 2001 with ATCC does not overcome the fundamental failure of Awasthi 2001 to anticipate each and every element of independent and amended claim 1 or amended claim 1 on its whole. Applicants further submit that ATTC does not suggest or teach contacting one or more cells with an antibody to ralA biding protein1, wherein the direct contact is cytotoxic to one or more cells in the absence of an additional agent. Thus, combining ATTC with Awasthi 2001 does not overcome the deficiencies of Awasthi 2001 as described above nor does the combination teach Applicants claimed invention on its whole. Moreover, Applicants assert that there is no teaching or suggestion in Awasthi 2001 or in ATCC to modify or combine the references in such a way that would resemble Applicants' invention as claimed in amended claim 1; nor is there any indication of a reasonable expectation of success if such references were to be combined.

These arguments have been carefully considered, but are not found persuasive.

First, Applicants arguments pertaining to Awasthi 2001 not anticipating amended claim 1 have been addressed above. Regarding Applicants assertion that ATTC does not suggest or teach contacting one or more cells with an antibody to ralA binding protein1, the Examiner acknowledges that ATCC does not explicitly teach contacting one or more cells with an antibody to ralA binding protein 1. However, the Examiner recognizes that it must be remembered that the references are relied upon in combination and are not meant to be considered separately as in a vacuum. It is the combination of all of the cited and relied upon references which make up the state of the art with regard to the claimed invention. Furthermore, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference and it is not that the claimed invention must be expressly suggested in any one or all of the references; but rather the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In the instant case, the suggestion to combine was based on the commercial availability of the tumor cell lines obtained from SCLC and NSCLC and the suggestion by Awasthi 2001 that SCLC and NSCLC cell lines undergoing uncontrolled cell growth are treated with RLIP76 antibodies which specifically recognize an epitope in lung cancer cells. Therefore,

Applicant's claimed invention fails to patentably distinguish over the state of the art represented by the cited references taken in combination.

Claims 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Awasthi *et al.* (Proc. Am. Assoc. Cancer. Res. March 2001; 42: Abst. *of record*) in view of American Type Culture Collection (Tumor Cell Lines, 2001 *of record*) in further view of Sause WT (Chest, 1999; 116: 504S-508S *of record*).

Awasthi *et al.* the American Type Culture Collection, applied to claims 1-2 and 4-9 above, teach a method of treating both SCLC and NSCLC cell lines undergoing uncontrolled growth comprising contacting the cells with RLIP76 antibodies which recognize a cell surface epitope in lung cancer cells, wherein ant-RLIP76 promotes apoptosis in the cell.

Awasthi *et al.* the American Type Culture Collection do not teach that the antibody is added in combination with radiation therapy.

Sause teaches the role of radiotherapy in non-small cell lung cancer. Specifically, the reference teaches that radiation therapy (RT) is an effective method of local disease control for non-small lung cancer (NSCLC) and can be used for definitive management in selected patients (page 504S, 1st column, 1st paragraph).

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the references so as to treat one or more cells undergoing uncontrolled growth. One of skill in the art would have been motivated to so because each of the therapeutics had been individually taught in the prior art to be successful at treating cells undergoing uncontrolled growth such as cancer. The instant situation is amenable to the type of analysis set forth in In re Kerkhoven,205 USPQ 1069 (CCPA 1980) wherein the court held that it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order to for a third composition that is to be used for the very same purpose since the idea of combining them flows logically from their having been individually taught in the prior art. Applying the same logic to the instant method claims, one of ordinary skill in the art would have reasonably expected that by adding RLIP76 antibodies in combination with radiation therapy, one would achieve an enhanced method of treating cell undergoing uncontrolled growth.

Moreover, the strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Sernaker, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983).

In response to this rejection, Applicants contend that claims 1-11 are not anticipated by Awasthi 2001 for the reasons set forth above. Thus, Applicants assert that combining Awasthi 2001 with Sause does not overcome the failure of Awasthi 2001 to teach amended claim 1. Moreover, Applicants submit that claim 1 does not tech adding RLIP in combination with radiation therapy, and therefore, combining Sause does not overcome the failures of Awasthi 2001. For example, Applicants argue that Sause does not suggest or teach contacting one or more cells with an antibody to ralA binding protein 1, wherein the direct contact is cytotoxic to one or more cells in the absence of an additional agent. Moreover, Applicants assert that there is no teaching or suggestion in Awasthi 2001 and Sause to modify or combine the references in such a way that would resemble Applicant's invention as claimed in amended claim 1; nor is there any indication of a reasonable expectation of success if such references were to be combined. Accordingly, Applicants submit that amended claims 1 and its dependents are patentably distinct from the cited art.

These arguments have been carefully considered, but are not found persuasive.

First, Applicants arguments pertaining to Awasthi 2001 not anticipating amended claim 1 have been addressed above. Regarding Applicants assertion that Sause does not suggest or teach contacting one or more cells with an antibody to ralA binding protein1, the Examiner acknowledges that Sause does not explicitly teach contacting one or more cells with an antibody to ralA binding protein1. However, the Examiner recognizes that it must be remembered that the references are relied upon in combination and are not meant to be considered separately as in a vacuum. It is the combination of all of the cited and relied upon references which make up the state of the art with regard to the claimed invention. Furthermore, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference and it is not that the claimed invention must be expressly suggested in any one or all of the references; but rather the test is what the combined teachings of the references would have suggested to those of

ordinary skill in the art. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In the instant case, one of skill in the art would have been motivated to combine the two references because each of the therapeutics had been individually taught in the prior art to be successful at treating cells undergoing uncontrolled growth such as cancer. As such, the instant situation is amenable to the type of analysis set forth in In re Kerkhoven,205 USPQ 1069 (CCPA 1980) wherein the court held that it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order to for a third composition that is to be used for the very same purpose since the idea of combining them flows logically from their having been individually taught in the prior art. Therefore, claims 1-11 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Awasthi *et al.* (Proc. Am. Assoc. Cancer. Res. March 2001; 42: Abs.) in view of Sause WT (Chest, 1999; 116: 504S-508S).

Claims 19-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen *et al.* (US 2002/0119156, 2001 *of record*) in combination with Awasthi *et al.* (Proc. Am. Assoc. Cancer. Res. March 2001; 42: Abst *of record.*).

Chen *et al.* teaches (abstract) antibodies immunospecific for polypeptides expressed in lung cancer, as well as methods for detecting, diagnosing, monitoring, staging and imaging lung cancer, i.e., cells undergoing uncontrolled growth. The publication further teaches (page 2, paragraph 0022) that the antibodies can be labeled with a variety of detectable labels including, not limited to, radioisotopes and paramagnetic metals. For example, Chen *et al.* discloses (page 13, paragraph 0154) that the labeled immunospecific antibodies can be injected into patients suspected of having lung cancer for the purposes of diagnosing and/or staging the disease status of the patient, wherein the amount of label within an organ or tissue allows for the determination of the presence or absence of cancer in that organ or tissue.

Chen *et al.* does not teach that the antibody is specific for RLIP76.

Awasthi *et al.* teaches an antibody to RLIP76, which specifically recognizes a cell surface epitope in lung cancers.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to label an antibody to RLIP76 as taught by Awasthi *et al.* for the purposes of identifying a cell undergoing uncontrolled growth as taught by Chen *et al.*. One would have

been motivated to do so because Awasthi *et al.* provides antibodies which specifically recognizes a cell surface epitope, RLIP76, in lung cancer cells. Thus, one of ordinary skill in the art would have a reasonable expectation of success that by combing anti-RLIP as taught by Awasthi et al. with the method taught by Chen et al., one would achieve a method of determining the presence or absence of lung cancer.

Therefore, NO claim is allowed.

***Conclusion***

This is a continuation of applicant's earlier Application No. 10/714,506. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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